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Stereoselective Synthesis of Functionalized 1,4-Dienes

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Abstract: The article reports a stereoselective synthesis of functionalized 1,4-dienes **5**, **6** by coupling allylic Baylis–Hillman acetates **1** and vinyl magnesium chloride at low temperature and in the presence of a catalytic amount of $LiCuBr_2$ (3%).

Keywords: Baylis–Hillman acetates, conjugate addition, functionalized 1,4-dienes

INTRODUCTION

We have previously reported the substitution of Baylis–Hillman acetates of type **1** by various nucleophilic reagents (i.e., Grignard and Gilman reagents, lithium ester enolates,[1] 1,3-diketone salts,[2] primary and secondary amines,[3] and sodium nitronates).[4] This procedure provides a solid carbon–carbon bond-forming reaction in organic chemistry, leading to a reliable method of obtaining some biologically active compounds (α-methylene-δ-valerolactones **2**,[1] (±)-sarkomycin **3**,[5] and (±)-mitsugashwalactone **4**[6]) (Scheme 1).

In addition to these methods for the introduction of a hydrocarbon group to the β-position of activated esters or ketones **1**,[7] we show that organocuprates, prepared in situ without additives, are selective reagents in the synthesis of functionalized 1,4-dienes **5**. The chemistry of functionalized 1,3- and 1,4-dienes has drawn particular attention because of their various applications in the synthesis of natural products, such as

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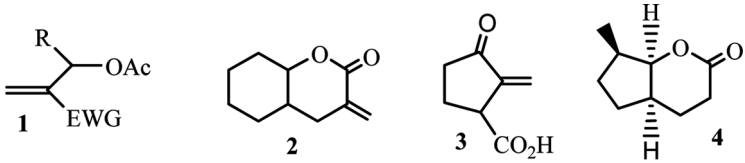
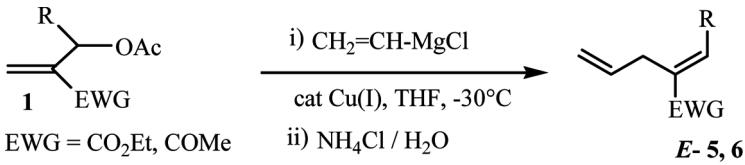


EWG = CO_2Et, COMe

Scheme 1.

terpenoids and carotenoids. In the case of the first class of dienes, previous syntheses include multistep protocols commencing from methyl pyruvate and ethyl acrylate,[8] Pd-catalyzed carbonylation of alkynediols,[9] pyrolysis of 1,2-diacetoxycyclobutene,[10] Stobbe condensation in a straightforward manner of dimethyl itaconate-anthracene then pyrolysis,[11] bismethylenation of the succinic ester phosphonate,[12] nickel(0)-catalyzed coupling reaction of α-halomethyl acrylate,[13] addition–elimination of nitronate salt to dimethyl α-(bromomethyl) fumarate,[14] and conjugate elimination on unsaturated acetals.[15] Furthermore, the homologous 1,4-dienes have been investigated extensively: several tandem reactions coupling readily available *E* allylic and homoallylic sulfones and aldehydes,[16] chelation-controlled reduction of benzothiazole β-oxosulfides,[17] cross-coupling reaction of 2-benzensulfonyl 1,4-dienes and alkyl magnesium under transition-metal catalysis,[18] and addition of functionalized allylic bromides to terminal alkynes.[19] Herein, we report findings on the stereoselective synthesis of the functionalized 1,4-dienes **5**, **6** in order to obtain new terminal functionalized 1,4-dienes in a simple one-pot and atom-economical procedure (Scheme 2).



EWG = CO_2Et, COMe

***E*- 5, 6**

Scheme 2.

RESULTS AND DISCUSSION

Commercial vinyl magnesium chloride was selected as a nucleophilic Grignard reagent to carry out conjugate addition of organocopper to the allylic Baylis–Hillman acetates **1**. The reaction of this reagent and **1**

(1:1.1–1.5 ratio) in tetrahydrofuran (THF) at $-30\,^{\circ}C$ in the presence of a catalytic amount of $LiCuBr_2$ (3%) gives, after quenching with aqueous ammonium chloride, the desired functionalized 1,4-dienes **5** or **6** in satisfactory yields and total stereoselectivity with 100%-*E* isomer based on spectroscopic evidence (downfield position of the vinylic proton $\delta > 6.50$ ppm in the trisubstituted ethylenic moiety).[20,21] First, the catalytic activity of Cu(I) including CuCl, CuBr, and CuI was tested. It seemed to be effective, but their solubility and the reaction complexity were globally inconclusive. Thus, the use of the lithium dibromocuprate ($LiCuBr_2$) as catalyst in the reaction medium significantly accelerates the overall rate of the reaction. This catalytic method was applied to various Grignard reagents as illustrated in Table 1.

Table 1. Synthesis of functional 1,4-dienes **5a–f** and **6a,b**

Entry	EWG	R	Time (min)	1,4-diene	Yield (%)
1	CO_2Et	CH_3	10	**5a**	52
2	CO_2Et	C_2H_5	15	**5b**	50
3	CO_2Et	$^{n}C_3H_7$	20	**5c**	71
4	CO_2Et	$^{i}C_3H_7$	25	**5d**	47
5	CO_2Et	$^{i}C_4H_9$	25	**5e**	59
6	CO_2Et	C_6H_5	20	**5f**	60
7	COMe	CH_3	20	**6a**	41
8	COMe	C_6H_5	20	**6b**	48

In conclusion, this work reports an efficient substitution of the Baylis–Hillman acetates **1** by Grignard reagent in the presence of a catalytic amount of $LiCuBr_2$. The procedure has several advantages including good yields, short reaction time, total stereoselectivity, and simple workup.

EXPERIMENTAL

All the reactions involving anhydrous conditions were conducted in dry glassware under a nitrogen atmosphere. The solvents were distilled under nitrogen prior to use. Commercial Grignard reagent was titrated prior to use,[22] with 1 M solution of benzyl alcohol in anhydrous toluene and 2,2′-bipyridyl as indicator. Reactions were monitored by thin-layer chromatography (TLC) on silica-gel plates (Fluka kieselgel 60 F_{254}), Fluka Kieselgel 70–230 mesh was used for purification on column chromatography. ^{1}H and ^{13}C NMR (fully decoupled) were recorded on a Bruker AMX 300 in $CDCl_3$ as solvent with TMS as the internal standard.

Mass spectrometry was performed on an Autospec 200, Micromass (Waters) instrument.

Synthesis of Functional 1,4-Dienes 5, 6: Typical Procedure

In a 100-mL round-bottomed flask, fitted with a 25 mL pressure-equalizing addition funnel, 5 mmol of allylic acetate **1** diluted in THF (20 mL) and 0.15 mmol (0.15 mL) of a 1 M $LiCuBr_2$ solution were introduced. The mixture was stirred and cooled to $-30°C$, followed by the addition of the vinyl magnesium chloride during 20 min. After the addition, stirring was continued until the reaction was complete as monitored by TLC. The mixture was quenched with saturated NH_4Cl solution (15 mL), then extracted with ether (3×20 mL), and the combined organic layers were dried ($MgSO_4$) and evaporated under reduced pressure. The resulting oil was purified by chromatography on silica (AcOEt/hexane, 1:9).

(*E*)-Ethyl 2-Ethylidene Pent-4-enoate 5a

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.20 (t, 3H, $J = 6.99$ Hz, C*H*$_3$-CH_2OCO); 1.72 (d, 3H, $J = 6.96$ Hz, C*H*$_3$CH=C); 3.00 (d, 2H, $J = 5.88$ Hz, –C*H*$_2$–CH=); 4.11 (q, 2H, $J = 6.99$ Hz, CH_3C*H*$_2$OCO); 4.88–4.96 (m, 2H, C*H*$_2$=CH); 5.73 (m, 1H, CH_2=C*H*–CH_2–); 6.87 (q, 1H, $J = 6.96$ Hz, CH_3C*H*=C). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.20 (*C*H$_3$–CH_2O); 14.30 (*C*H$_3$–C=); 30.50 (*C*H$_2$–CH=); 60.60 (*C*H$_2$O); 114.90 (*C*H$_2$=); 131.00 (=*C*–CO); 135.20 (*C*H=CH_2); 137.50 (=*C*H–Me); 167.40 (*C*=O). HRMS calcd. for $C_9H_{14}O_2$: 154.0994; found: 154.0992.

(*E*)-Ethyl 2-Propylidene Pent-4-enoate 5b

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.05 (t, 3H, $J = 7.35$ Hz, C*H*$_3$CH$_2$CH=C–); 1.29 (t, 3H, $J = 6.99$ Hz, C*H*$_3$CH$_2$OCO); 2.21 (qd, 2H, $J = 7.35$ Hz, $J = 7.35$ Hz, CH_3C*H*$_2$CH=C–); 3.07 (d, 2H, $J = 5.88$ Hz, –C*H*$_2$–CH=); 4.19 (q, 2H, $J = 6.99$ Hz, CH_3C*H*$_2$OCO); 4.96–5.04 (m, 2H, C*H*$_2$=CH); 5.81 (m, 1H, CH_2=C*H*–CH_2–); 6.83 (t, 1H, $J = 7.35$ Hz, C=C*H*CH$_2$CH$_3$). ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.21 (*C*H$_3$–CH_2O); 14.16 (*C*H$_3$–CH$_2$); 21.89 (CH_3–*C*H$_2$–CH); 30.76 (*C*H$_2$–CH=); 60.46 (*C*H$_2$O); 114.95 (*C*H$_2$=); 129.45 (=*C*–CO); 135.67 (*C*H=CH_2); 145.14 (=*C*H–C_2H_5); 167.67 (*C*=O). HRMS calcd. for $C_{10}H_{16}O_2$: 168.1150; found: 168.1150.

(*E*)-Ethyl 2-Allyl Hex-2-enoate 5c

^{1}H NMR (300 MHz, $CDC1_3$): δ 0.95 (t, 3H, $J = 7.50$ Hz, $CH_3CH_2CH_2$); 1.29 (t, 3H, $J = 7.50$ Hz, CH_3CH_2OCO); 1.48 (qt, 2H, $J = 7.50$ Hz, $J = 7.50$ Hz, $CH_3CH_2CH_2$); 2.17 (dt, 2H, $J = 7.50$ Hz, $J = 7.50$ Hz, $CH_3CH_2CH_2$–CH=); 3.07 (d, 2H, $J = 7.50$ Hz, –CH_2–CH=); 4.19 (q, 2H, $J = 7.50$ Hz, CH_3CH_2OCO); 4.95–5.04 (m, 2H, CH_2=CH–CH_2); 5.79 (m, 1H, CH_2=CH–CH_2–); 6.84 (t, 1H, 7.50 Hz, C=CHCH_2CH_2). ^{13}C NMR (75 MHz, $CDCI_3$): δ 14.18 (CH_3–CH_2O); 14.23 (CH_3–CH_2); 22.71 (CH_3–CH_2–CH_2); 30.90 (CH_3–CH_2–CH_2); 31.63 (CH_2–CH=); 60.36 (CH_2O); 115.06 (CH_2=); 130.15 (=C–CO); 135.67 (CH=CH_2); 143.87 (=CH–Pr); 167.57 (C=O). HRMS calcd. for $C_{11}H_{18}O_2$: 182.1303; found: 182.1307.

(*E*)-Ethyl 2-(2-methylpropylidene) Pent-4-enoate 5d

^{1}H NMR (300 MHz, $CDC1_3$): δ 0.91 [d, 6H, $J = 6.82$ Hz, $(CH_3)_2$CH]; 1.20 (t, 3H, $J = 7.10$ Hz, CH_3CH_2OCO); 2.59 [m, 1H, $(CH_3)_2$–CH]; 2.98 (d, 2H, $J = 5.90$ Hz, –CH_2–CH=CH_2); 4.15 (q, 2H, $J = 7.10$ Hz, CH_3CH_2OCO); 4.91–5.01 (m, 2H, CH_2=CH–CH_2); 5.75 (m, 1H, CH_2=CH–CH_2–); 6.55 [d, 1H, $J = 7.30$ Hz, $(CH_3)_2$CH–CH=]. ^{13}C NMR (75 MHz, $CDC1_3$): δ 14.21 (CH_3–CH_2O); 22.99 [$CH(CH_3)_2$]; 28.34 [$CH(CH_3)_2$]; 32.47 (CH_2–CH=); 60.62 (CH_2O); 114.94 (CH_2=); 128.34 (=C–CO); 136.11 (CH=CH_2); 143.98 (=CH–^{i}Pr); 167.79 (C=O). HRMS calcd. for $C_{11}H_{18}O_2$: 182.1307; found: 182.1307.

(*E*)-Ethyl 2-Allyl-5-methyl Hex-2-enoate 5e

^{1}H NMR (300 MHz, $CDC1_3$): δ 0.86 [d, 6H, $J = 6.00$ Hz, $(CH_3)_2$CH]; 1.22 (t, 3H, $J = 7.50$ Hz, CH_3CH_2OCO); 1.69 [m, 1H, $(CH_3)_2$–CH–CH_2]; 2.01 [dd, 2H, $J = 7.50$ Hz, $J = 7.50$ Hz, $(CH_3)_2$–CH–CH_2–CH=]; 3.00 (d, 2H, $J = 6.00$ Hz, –CH_2–CH=CH_2); 4.13 (q, 2H, $J = 7.50$ Hz, CH_3CH_2OCO); 4.88–4.97 (m, 2H, CH_2 = CH–CH_2); 5.74 (m, lH, CH_2=CH–CH_2); 6.79 [t, 1H, $J = 7.50$ Hz, $(CH_3)_2$–CH–CH_2–CH=]. ^{13}C NMR (75 MHz, $CDC1_3$): δ 14.28 (CH_3–CH_2O); 23.07 [$CH(CH_3)_2$]; 28.82 [$CH(CH_3)_2$]; 30.90 (CH_2–CH=); 37.79 (CH_2–^{i}Pr); 60.61 (CH_2O); 115.01 (CH_2=); 130.45 (=C–CO); 135.58 (CH=CH_2); 142.71 (=CH–^{i}Bu); 167.60 (C=O). HRMS calcd. for $C_{12}H_{20}O_2$: 196.1463; found: 196.1463.

(*E*)-3-Ethyl 2-Benzylidene Pent-4-enoate 5f

^{1}H NMR (300 MHz, $CDC1_3$): δ 1.23 (t, 3H, $J = 7.00$ Hz, CH_3CH_2OCO); 3.18 (d, 2H, $J = 5.86$ Hz, –CH_2–CH=); 4.15 (q, 2H, $J = 7.00$ Hz,

CH_3CH_2OCO); 4.99–5.08 (m, 2H, CH_2=CH–CH_2–); 5.89 (m, 1H, CH_2=C*H*–CH_2); 7.23 (m, 5H, C_6H_5); 7.71 (s, 1H, Ph–C*H*=). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.28 (*C*H_3–CH_2O); 31.66 (*C*H_2–CH=); 60.81 (*C*H_2O); 116.56 (*C*H_2=); 128.57; 128.64; 129.01; 135.50 (C_6H_5); 130.49 (=*C*–CO); 135.70 (*C*H=CH_2); 140.17 (=*C*H–Ph); 167.91 (*C*=O). HRMS calcd. for $C_{14}H_{16}O_2$: 216.1150; found: 216.1150.

(*E*)-3-Ethylidene Hex-5-en-2-one 6a

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.88 (d, 3H, J = 6.92 Hz, C*H*$_3$–CH=C); 2.31 (s, 3H, *C*H_3CO); 3.06 (d, 2H, J = 5.86 Hz, –CH_2=CH–C*H*$_2$–C=); 4.95–5.03 (m, 2H, C*H*$_2$=CH–); 5.75 (m, lH, CH_2=C*H*); 6.85 (q,lH, J = 6.92 Hz, CH_3–C*H*=C). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.30 (*C*H_3–CH=); 25.16 (*C*H_3–CO); 29.27 (*C*H_2–CH=); 115.69 (*C*H_2=); 135.27 (*C*H=CH_2); 140.64 (CH_3–*C*H=); 141.21 (=*C*–CO); 198.59 (*C*=O). HRMS calcd. for $C_8H_{12}O$: 124.0862; found: 124.0888.

(*E*)-3-Benzylidene Hex-5-en-2-one 6b

^{1}H NMR (300 MHz, $CDCl_3$): δ 2.37 (s, 3H, C*H*$_3$CO); 3.17 (d, 2H, J = 5.86 Hz, CH_2=CH–C*H*$_2$–C=); 4.93–5.03 (m, 2H, C*H*$_2$=CH); 5.86 (m, 1H, CH_2=C*H*–CH_2); 7.30 (m, 5H, C_6H_5); 7.58 (s, 1H, Ph–C*H*=). ^{13}C NMR (75 MHz, $CDCl_3$): δ 26.18 (*C*H_3–CO); 32.46 (*C*H_2–CH=); 117.09 (*C*H_2=); 128.25; 128.98; 129.50; 129.81 (C_6H_5); 135.11 (*C*H=CH_2); 139.21 (*C*H–Ph); 141.20 (=*C*–CO); 199.64 (*C*=O). HRMS calcd. For $C_{13}H_{14}O$: 186.1045: found: 186.1045.

REFERENCES

1. (a) Amri, H.; Rambaud, M.; Villiéras, J. Esters α-méthyléniques par substitution d'éthers et d'acétates dérivés de l' α-(hydroxyméthyl) acrylate d' éthyle. *J. Organomet. Chem.* **1990**, *384*, 1–11; (b) Amri, H.; Rambaud, M.; Villiéras, J. Substitution nucléophile d'acétates de cyclénols allyliques fonctionnels par des organométalliques en présence de sels cuivreux: Application à une synthèse rapide de la (±) mistugashiwalactone. *Tetrahedron* **1990**, *46*, 3535–3546.
2. Beltaïf, I.; Amri, H. Substitution of allylic functional acetates: Stereoselective synthesis of 2-alkylidene-1,5-ketoesters. *Synth. Commun*. **1994**, *24*, 2003–2010.
3. Amri, H.; El Gaïed, M. M.; Ben Ayed, T.; Villiéras, J. Synthèse de γ-lactames et de perhydro-1,2-pyridazin-3-ones polyfonctionnels. *Tetrahedron Lett*. **1992**, *33*, 6159–6160.

4. Chamakh, A.; M'hirsi, M.; Villiéras, J.; Lebreton, J.; Amri, H. A simplified route to the (E)-2-alkylidene-1,4-diketones. *Synthesis* **2000**, *2*, 295–299.
5. Amri, H.; Rambaud, M.; Villiéras, J. A short large-scale synthesis of (±) sarkomycin esters. *Tetrahedron Lett*. **1989**, *30*, 7381–7382.
6. Amri, H.; Rambaud, M.; Villiéras, J. Alkylation d'acétates de cyclénols fonctionnels (5 et 6) chaînons par les réactifs de Grignard et les énolates lithiens catalysée (ou non) par les sels de cuivre (I): Synthèse rapide de la (±)-mitsugashiwalactone. *Tetrahedron Lett*. **1987**, *28*, 5521–5524.
7. Basavaiah, D.; Rao, P. D.; Hyma, R. S. The Baylis–Hillman reaction: A novel carbon–carbon bond forming reaction. *Tetrahedron* **1996**, *52*, 8001–8062.
8. Grundke, C.; Hoffmann, H. M. R. Dimethyl 2,3-dimethylenebutanedioate from methyl pyruvate and methyl acrylate. *Chem. Ber*. **1987**, *120*, 1461–1462.
9. Kiji, J.; Okano, T.; Fujii, E.; Tsuji, J. A simple synthetic method to bis (methylene)butanedioates. *Synthesis* **1997**, 869–870.
10. Belluš, D.; Weis, C. D. A facile synthesis of 2,3-dicyanobutadiene-1,3 and 2,3-dicarbomethoxybutadiene-1,3. *Tetrahedron Lett*. **1973**, *14*, 999–1000.
11. Tarnchompoo, B.; Thebtaranonth, C.; Thebtaranonth, Y. 2,3-Dicarbomethoxy-1,3-butadiene and its reactions. *Tetrahedron Lett*. **1987**, *28*, 6671–6674.
12. Davidson, R. M.; Kenyon, G. L. J. Analogs of phosphoenol pyruvate, 3: New synthetic approaches to alpha-(dihydroxyphosphinylmethyl) acrylic acid and unequivocal assignments of the vinyl protons in its nuclear magnetic resonance spectrum. *J. Org. Chem*. **1977**, *42*, 1030–1035.
13. Belluš, D.; Bredow, K. V.; Sauter, H.; Weis, C. D. Synthesis and reactivity of 4-ring compounds 1-(4 + 2)-cycloadditions of 1,2-dicyanocyclobutene and its thermal ring-opening to 2,3-dicyanobuta-1,3-diene. *Helv. Chim. Acta* **1973**, *56*, 3004–3038.
14. Béji, F.; Lebreton, J.; Villiéras, J.; Amri, H. A total stereospecific route to α-alkylidene-γ-lactames. *Tetrahedron* **2001**, *57*, 9959–9962.
15. Maddaluno, J.; Gaonac'h, O.; Le Gallic, Y.; Duhamel, L. Conjugate-elimination on unsaturated acetals: A one-step route to functionalized 1,3-dienes. *Tetrahedron Lett*. **1995**, *36*, 8591–8594.
16. (a) Cuvigny, T.; Hervé du Penhoat, C.; Julia, M. Syntheses using sulfones XVIII: Use of 1,1-disulfones for the stereoselective synthesis of unsaturated compounds. *Bull. Soc. Chim. France* **1982**, *2*, 43–51; (b) Cuvigny, T.; Hervé du Penhoat, C.; Julia, M. Syntheses with sulfones XLVI: Stereoselective preparation of 2-benzenesulfonyl-1,3-dienes and 2-benzenesulfonyl-1,4-dienes. *Tetrahedron* **1986**, *42*, 5329–5336; (c) Hervé du Penhoat, C.; Julia, M. Synthesis with sulfones XLIV: Stereoselective preparation of EE 1,3-dienes by elimination of benzenesulfinic acid from E homoallylic sulfones. *Tetrahedron* **1986**, *42*, 4807–4816.
17. Caló, V.; Nacci, A. Stereoselective synthesis of 1,4-dienes by chelation-controlled reduction of benzothiazole β-oxosulfides. *Tetrahedron Lett*. **1998**, *39*, 3825–3828.
18. Alvarez, E.; Cuvigny, T.; Hervé du Penhoat, C.; Julia, M. Syntheses with sulfones XLVIII: Stereoselective synthesis of 2-isopropyl 1,4-dienes through the

iron-catalysed cross-coupling reaction of 2-benzenesulfonyl 1,4-dienes and isopropylmagnesium chloride. *Tetrahedron* **1988**, *44*, 111–118.
19. (a) Knochel, P.; Normant, J. F. Addition of functionalized allylic bromides to terminal alkynes. *Tetrahedron Lett*. **1984**, *25*, 1475–1478; (b) Knochel, P.; Normant, J. F. Synthèse de dièmes-1,4 fonctionnalisés par addition de zinciques allyliques fonctionnalisés sur des alcynes vrais et leur cyclisation en hétérocycles ou carbocycles. *J. Organomet. Chem*. **1986**, *309*, 1–23, and references cited therein.
20. Bull, L. B.; Culvenor, C. C. J.; Dick, A. T. *The pyrolizidine Alkaloids*; North Holland Publishing Co.: Amsterdam, **1968**.
21. (a) Pascual, C.; Meier, J.; Simon, W. Regel zur Abschätzung der chemischen Verschiebung von Protonen an einer Doppelbindung. *Helv. Chim. Acta* **1966**, *49*, 164–168; (b) Matter, U. E.; Pascual, C.; Pretsch, E.; Simon, W.; Sternhell, S. Estimation of the chemical shifts of olefinic protons using additive increments II: The compilation of additive increments for 43 functional groups. *Tetrahedron* **1969**, *25*, 691–697.
22. Watson, S. C.; Eastham, J. F. Colored indicators for simple direct titration of magnesium and lithium reagents. *J. Organomet. Chem*. **1967**, *9*, 165–168.